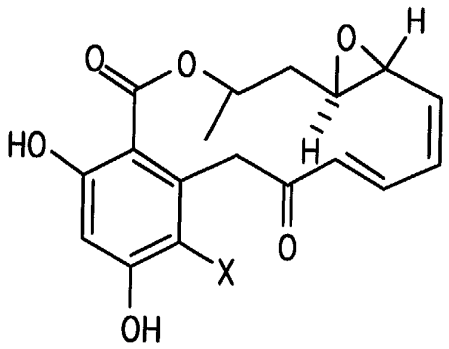
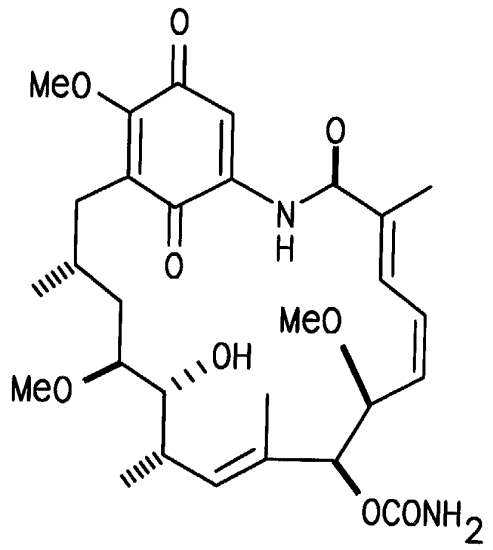
FIG. 1



X=Cl Radicicol (1)

X=H Monocillin I (2)



Geldanamycin (3)

FIG.2

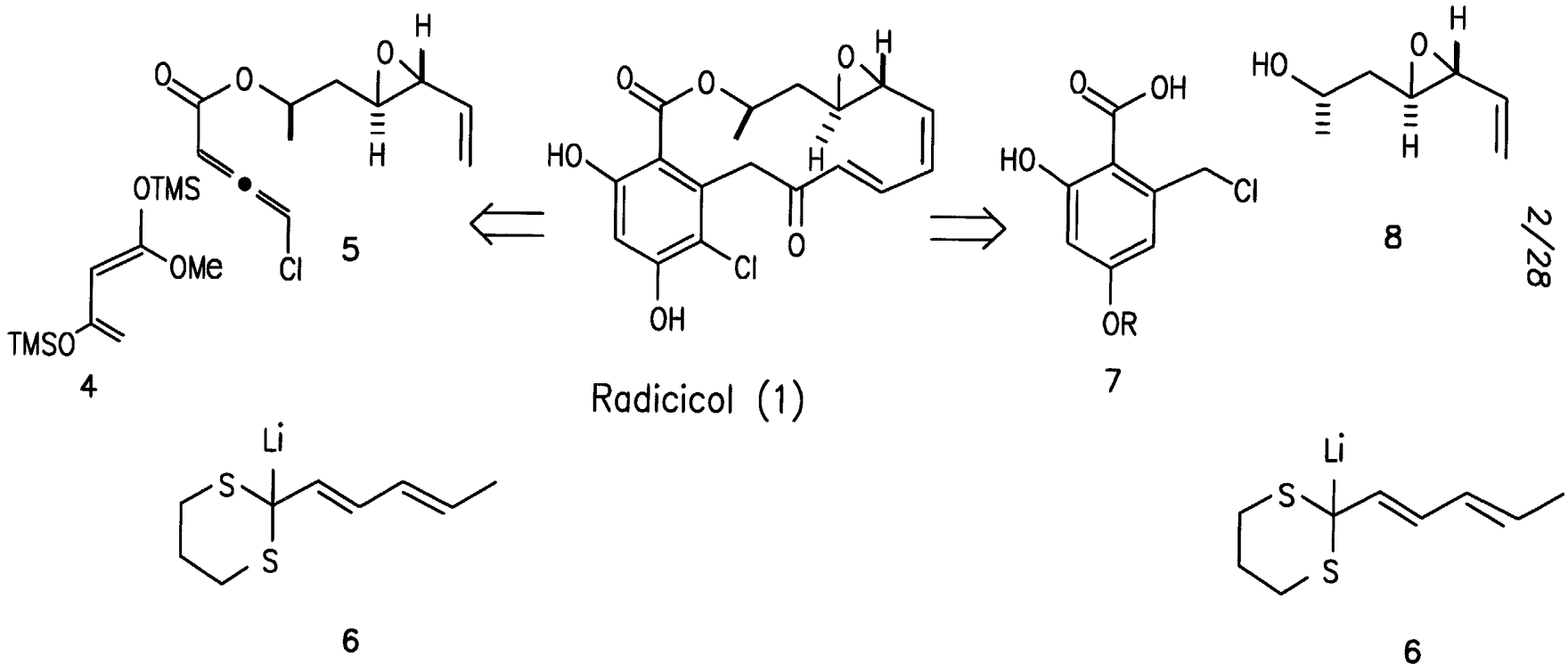
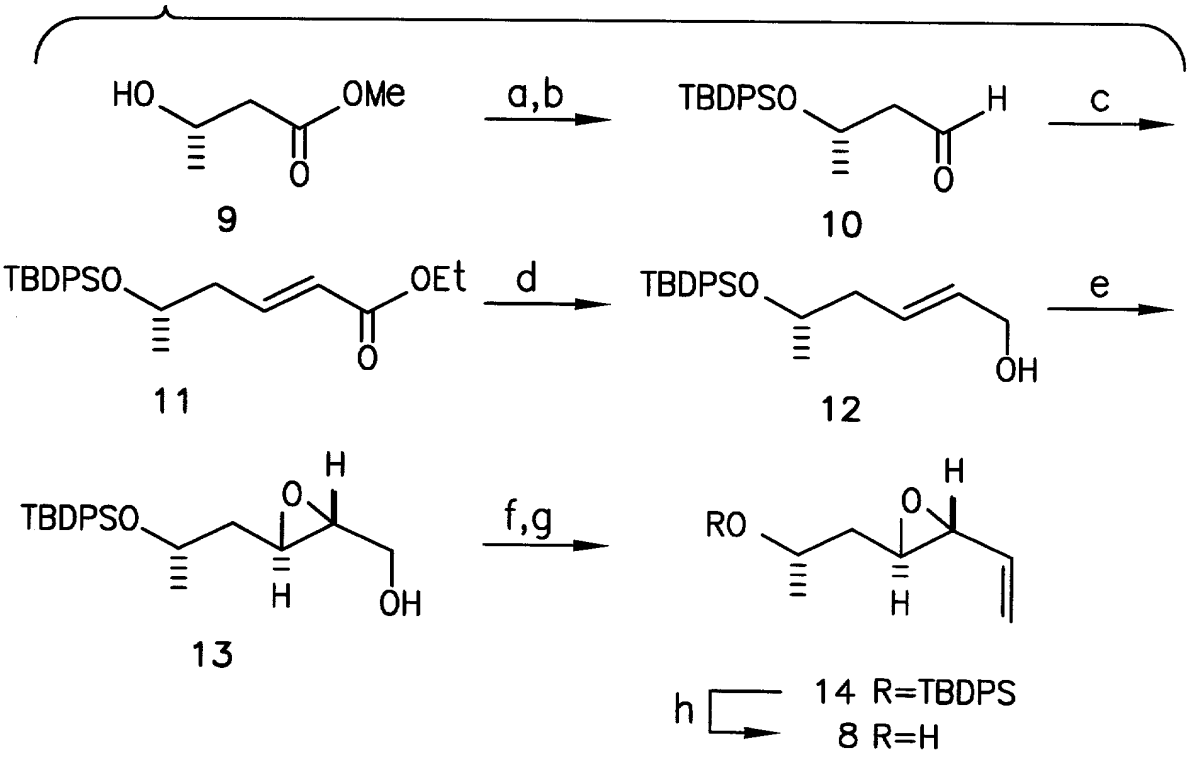
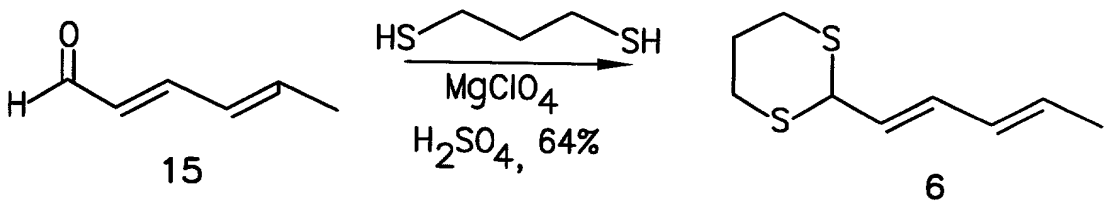


FIG.3

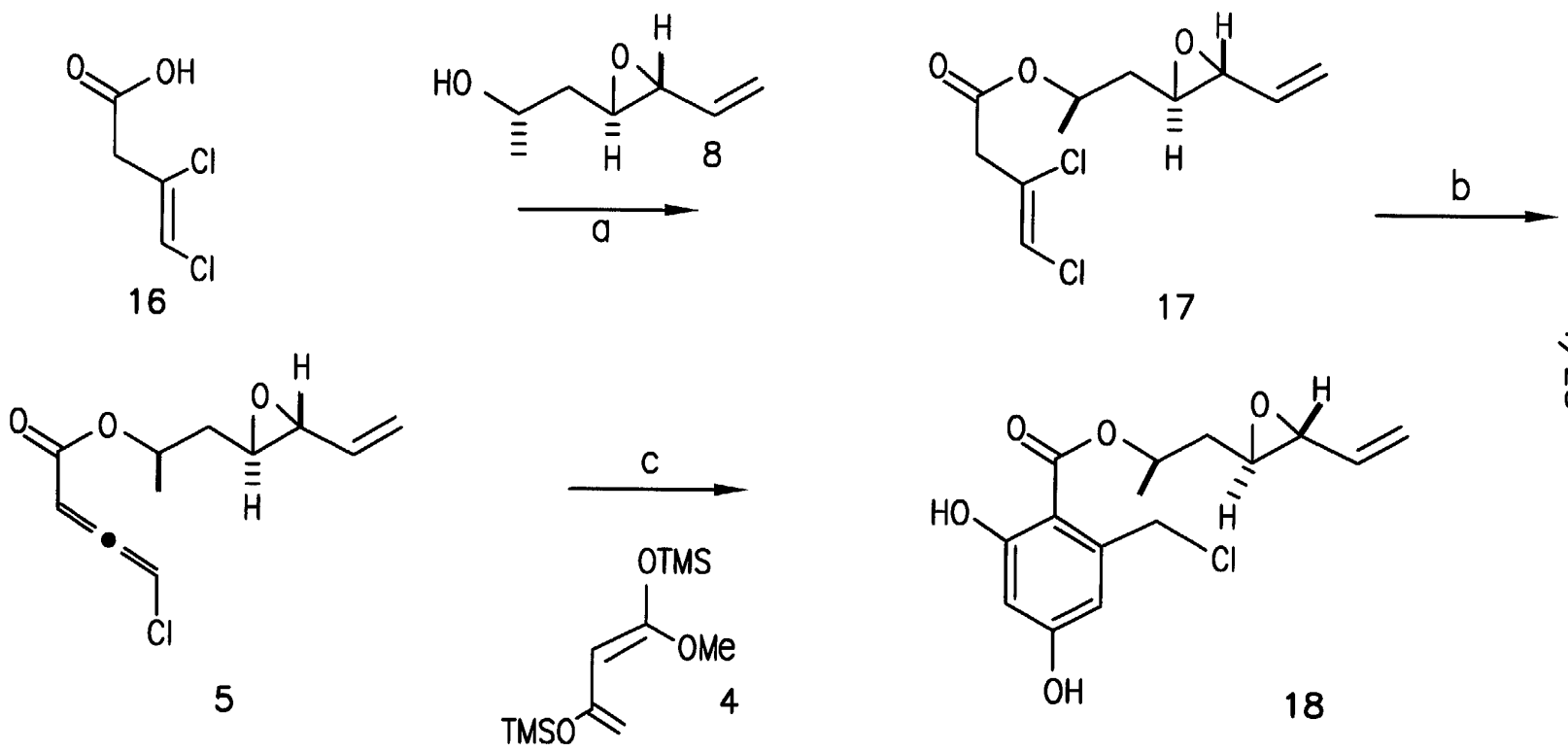


(a) TBDPSCl, imid.,>95%; (b) DIBAL–H,–78 °C, 92%;
(c) LiCl, DIPEA $(EtO)_2P(O)CH_2CO_2Et$, 95%;
(d) DIBAL–H, –20 °C, 96%; (e) (+)–DET, $Ti(OiPr_4)$, TBHP,90%,>95%ee; (f) SO_3*pyridine, Et_3N, DMSO, 90%;
(g) PH_3PCH_3Br, NaHMDS, 0 °C, 82%; (h) TBAF, 89%.



15 6

FIG. 4



(a) DEAD, PPh_3, 70%; (b.) iPr_2NEt, 70%; (c.) 50% (4:1)

FIG.5

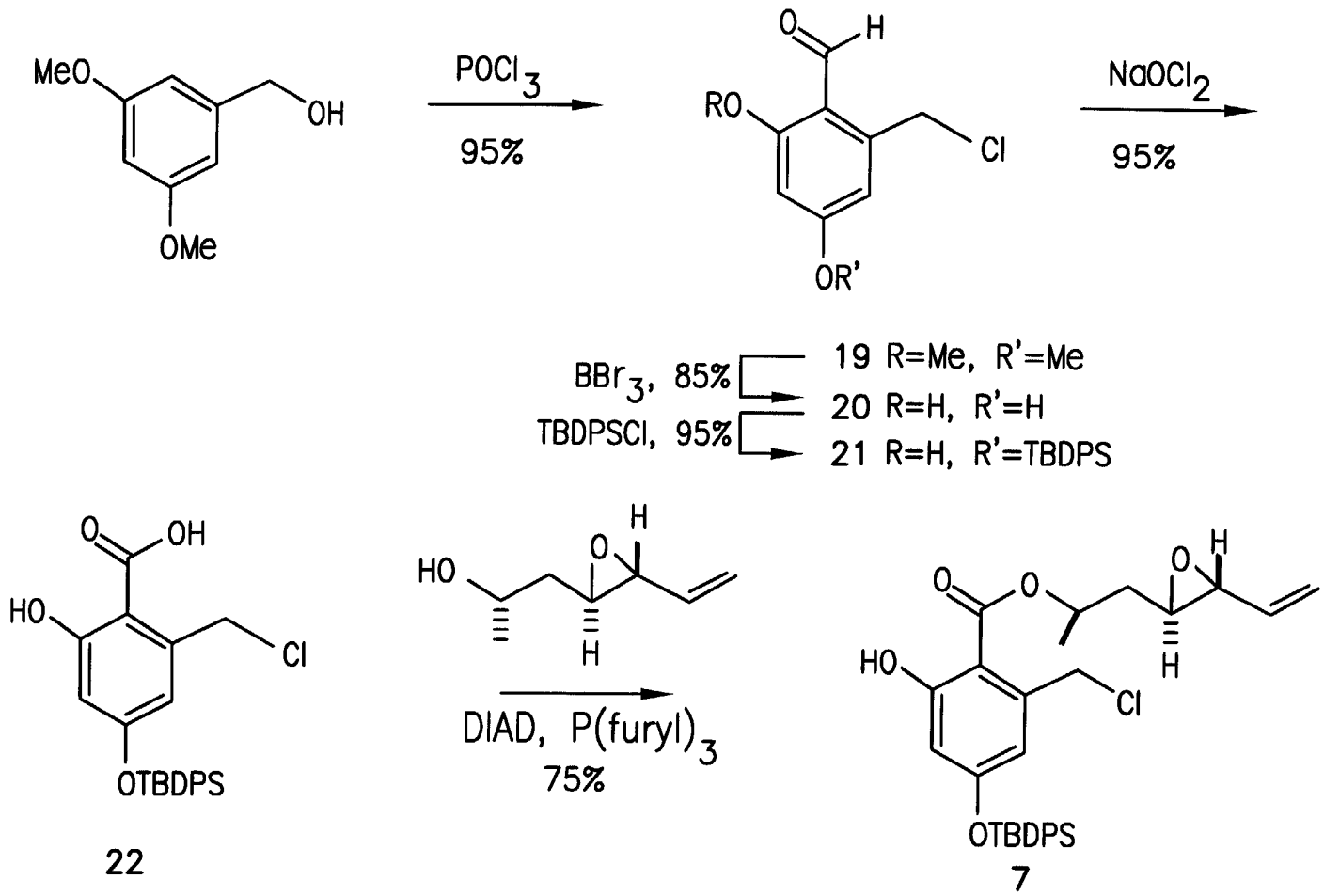
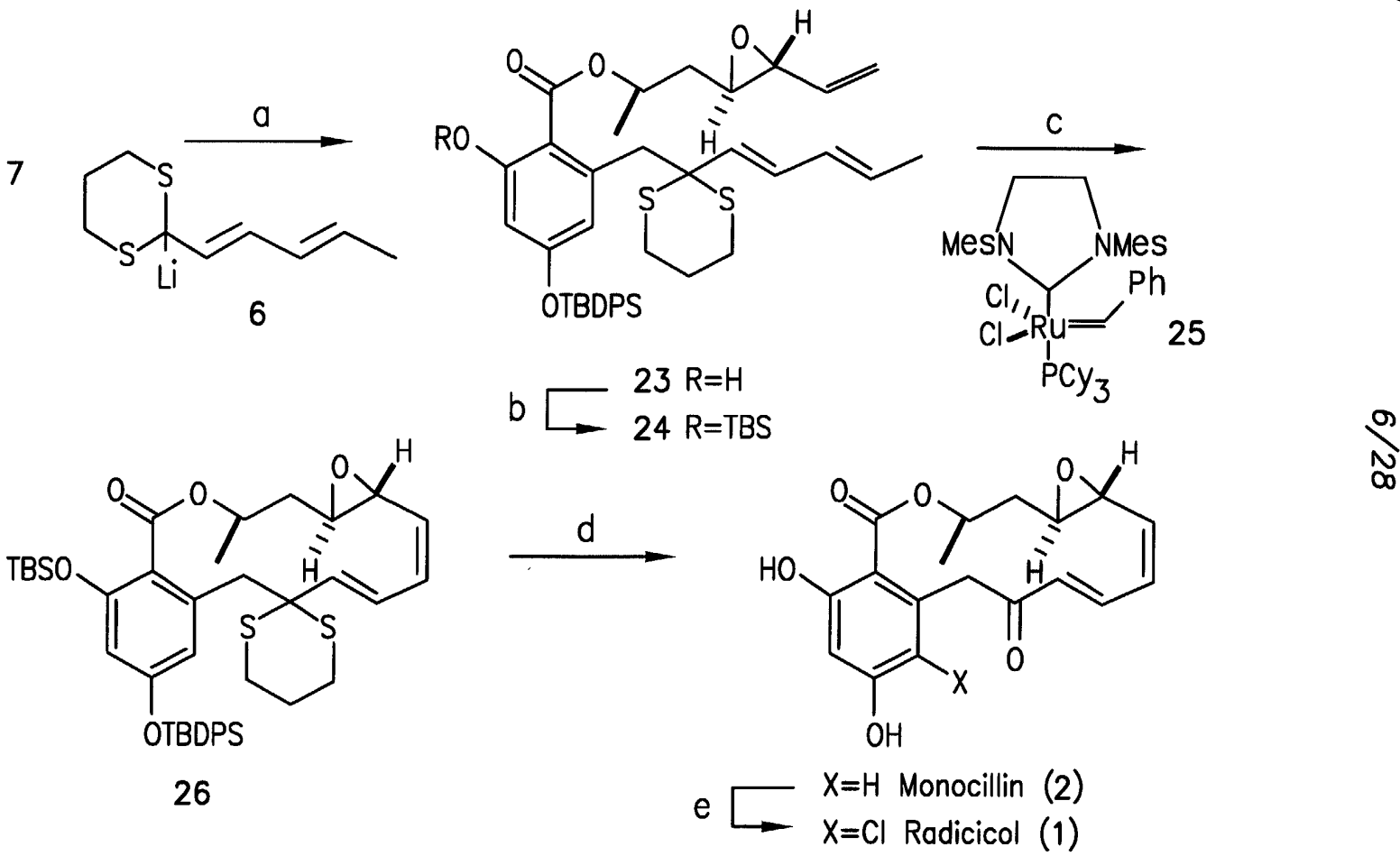

MeO
OH
OMe
POCl3
95%
O
H
RO
Cl
OR'
NaOCl2
95%
BBr3, 85%
19 R=Me, R'=Me
20 R=H, R'=H
TBDPSCl, 95%
21 R=H, R'=TBDPS
O
OH
HO
Cl
OTBDPS
22
HO
O
H
H
DIAD, P(furyl)3
75%
O
O
HO
Cl
OTBDPS
7

FIG. 6



a. n–BuLi, –78 °C, 50% (6:1); b. TBSCl, 83%; c. 42 C, 70%; d. (i) mCPBA, (ii) Ac_2O, Et_3N, H_2O, 60 °C, (iii) $NaHCO_3$, MeOH, 60%; e. SO_2Cl_2, 50%

FIG. 7

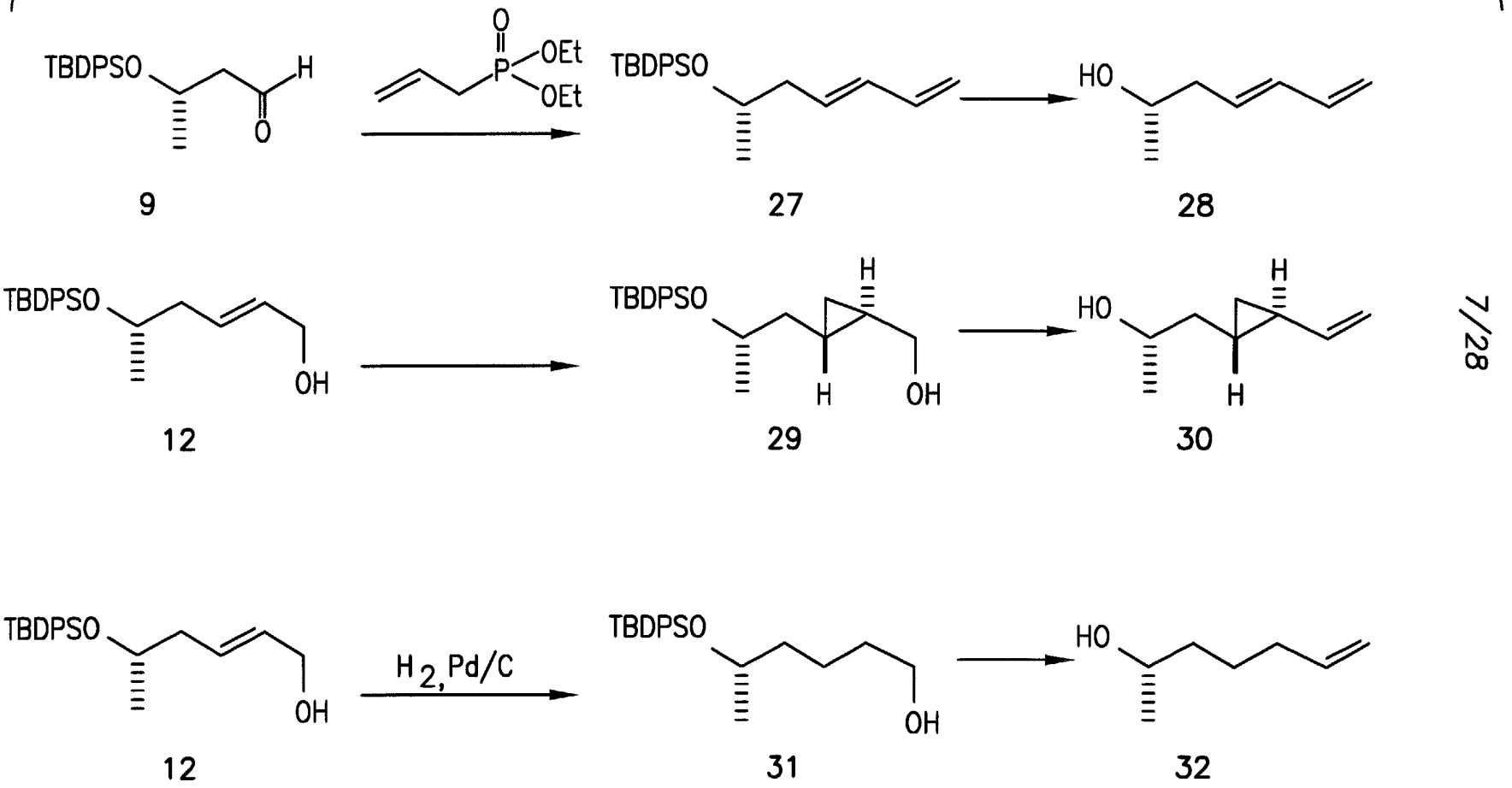
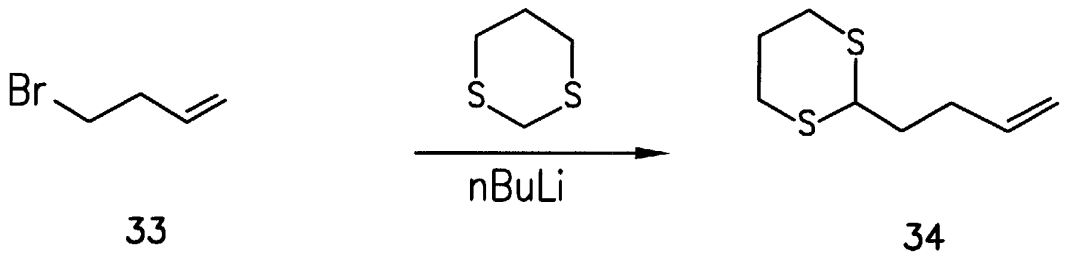

TBDPSO
H
O
9
O
P
OEt
OEt
TBDPSO
27
HO
28
TBDPSO
OH
12
TBDPSO
H
H
OH
29
HO
H
H
30
TBDPSO
OH
12
H2, Pd/C
TBDPSO
OH
31
HO
32

FIG.8



33 34

FIG.9

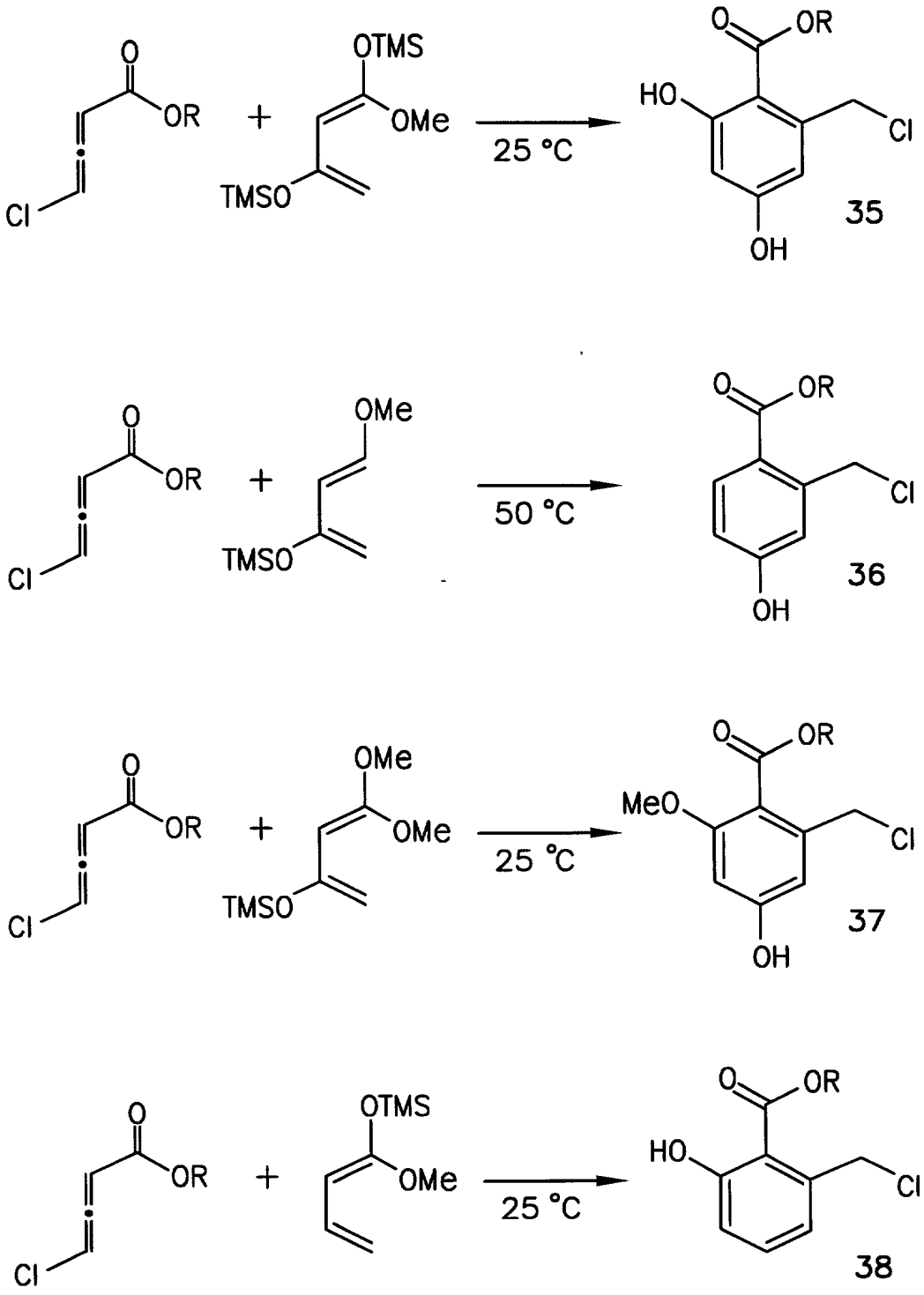
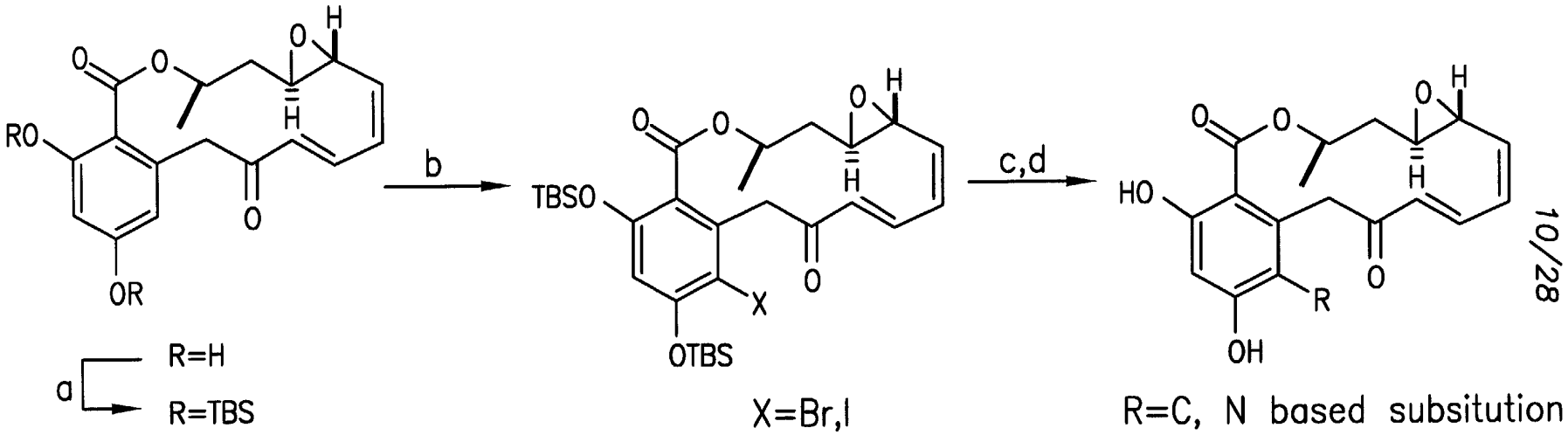
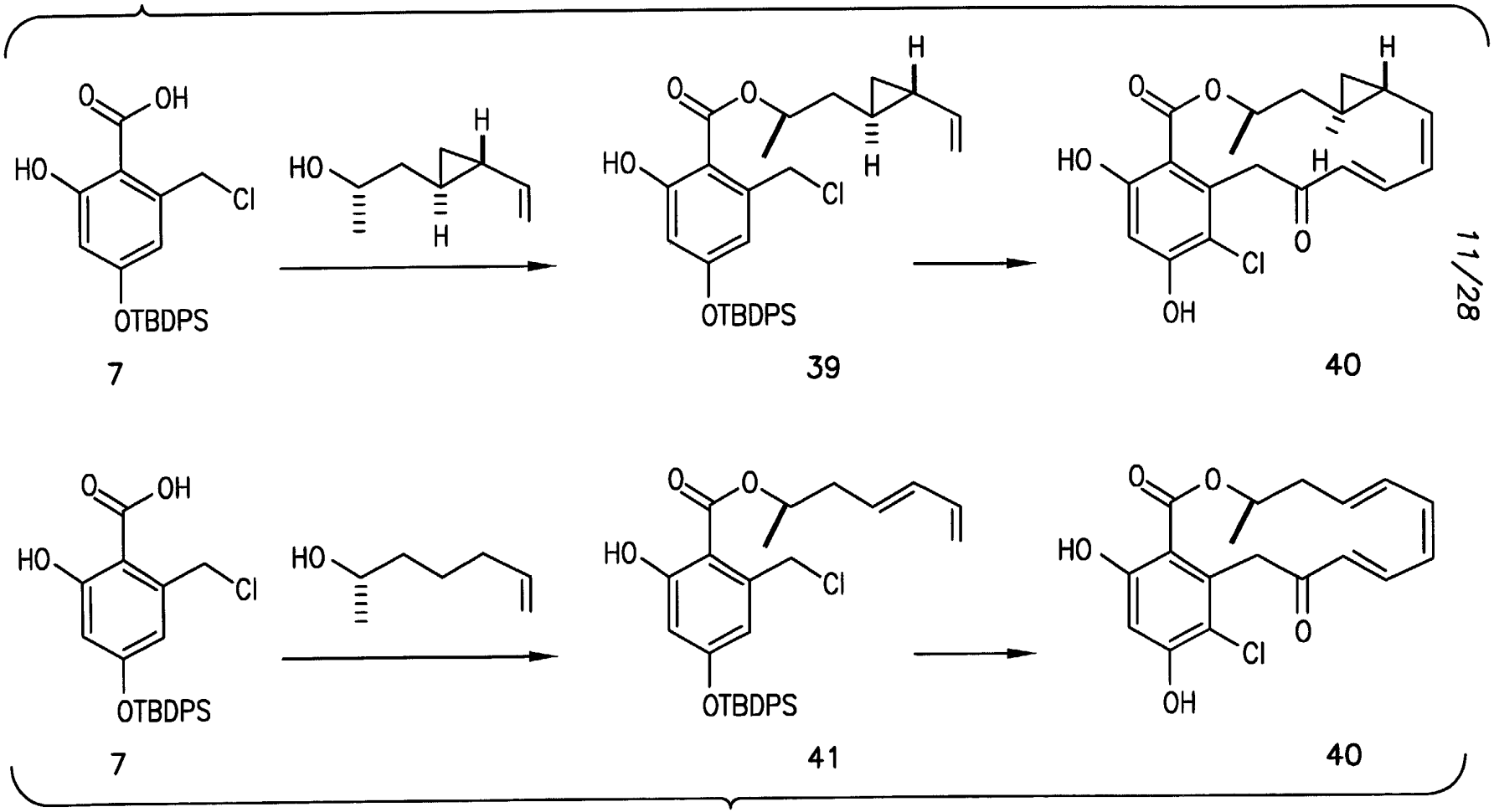


FIG. 10



a. TBSCl, pyridine; b. NIS or NBS, TsOH; c. $Pd(PPh)_3$, $RSnBu_3$, d. nBu_4NF

FIG. 11-1



TO FIG. 11-2

FROM FIG. 11-1

FIG. 11-2

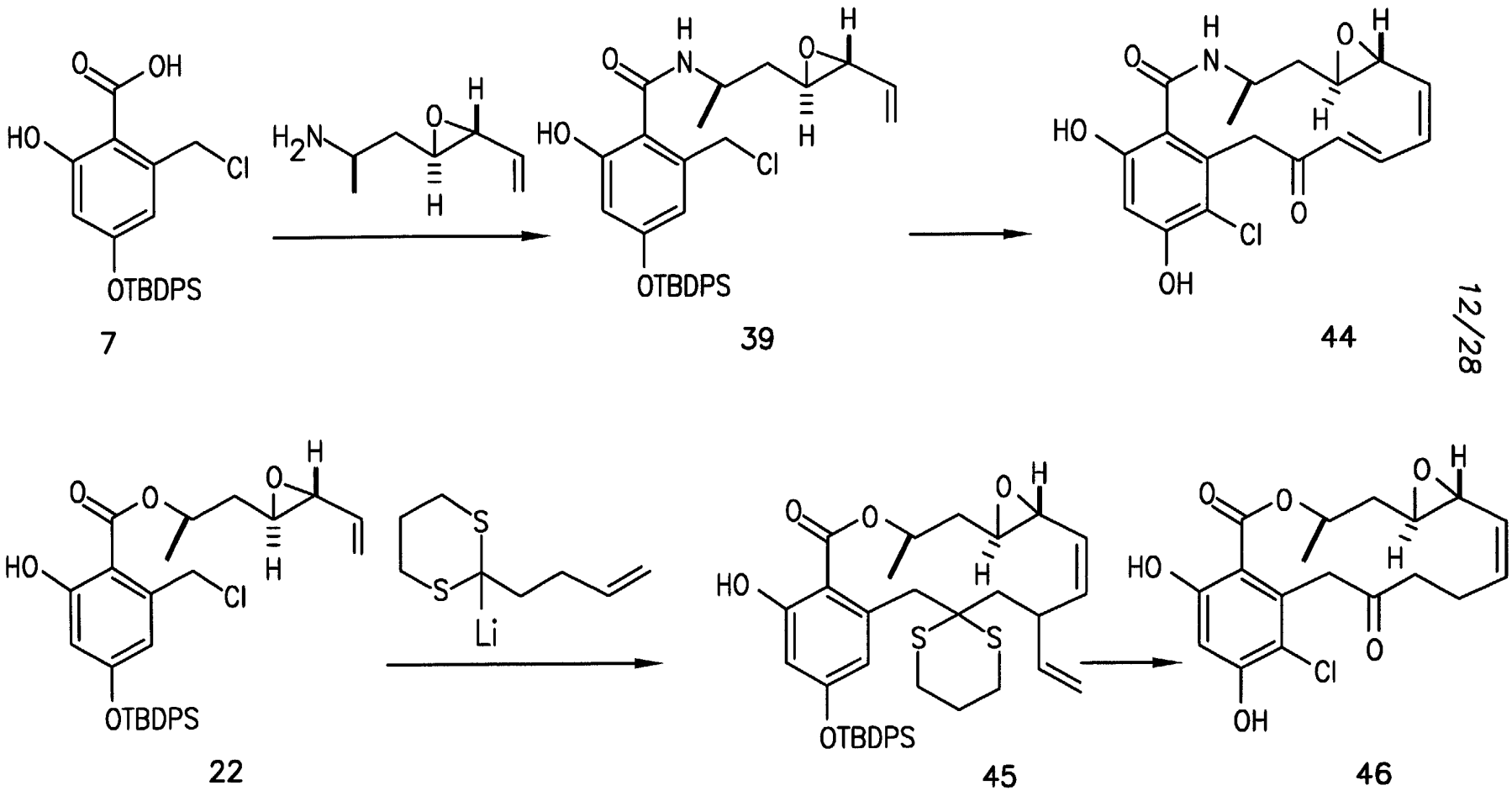
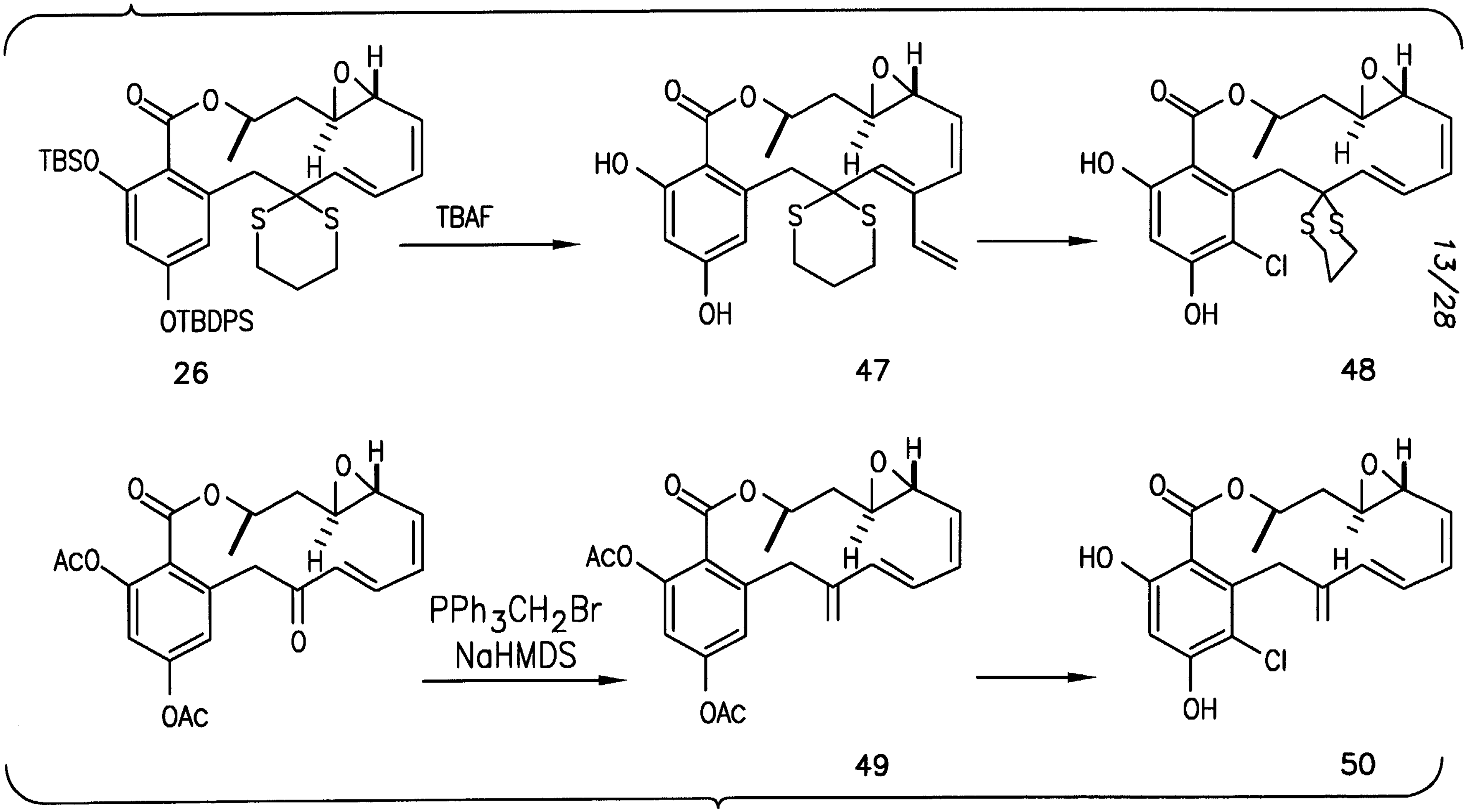


FIG. 12-1



TO FIG. 12-2

FROM FIG. 12-1

FIG. 12-2

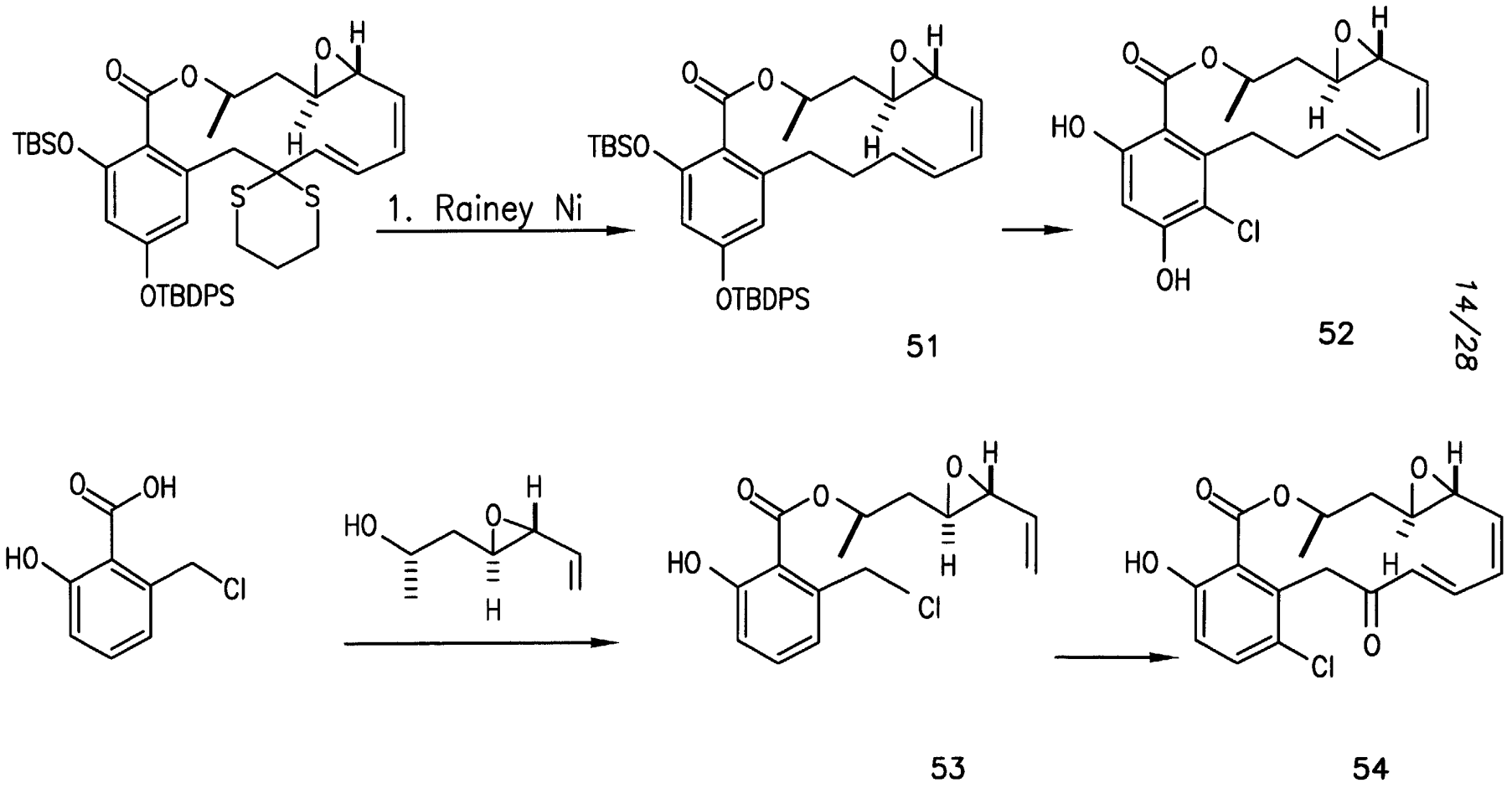
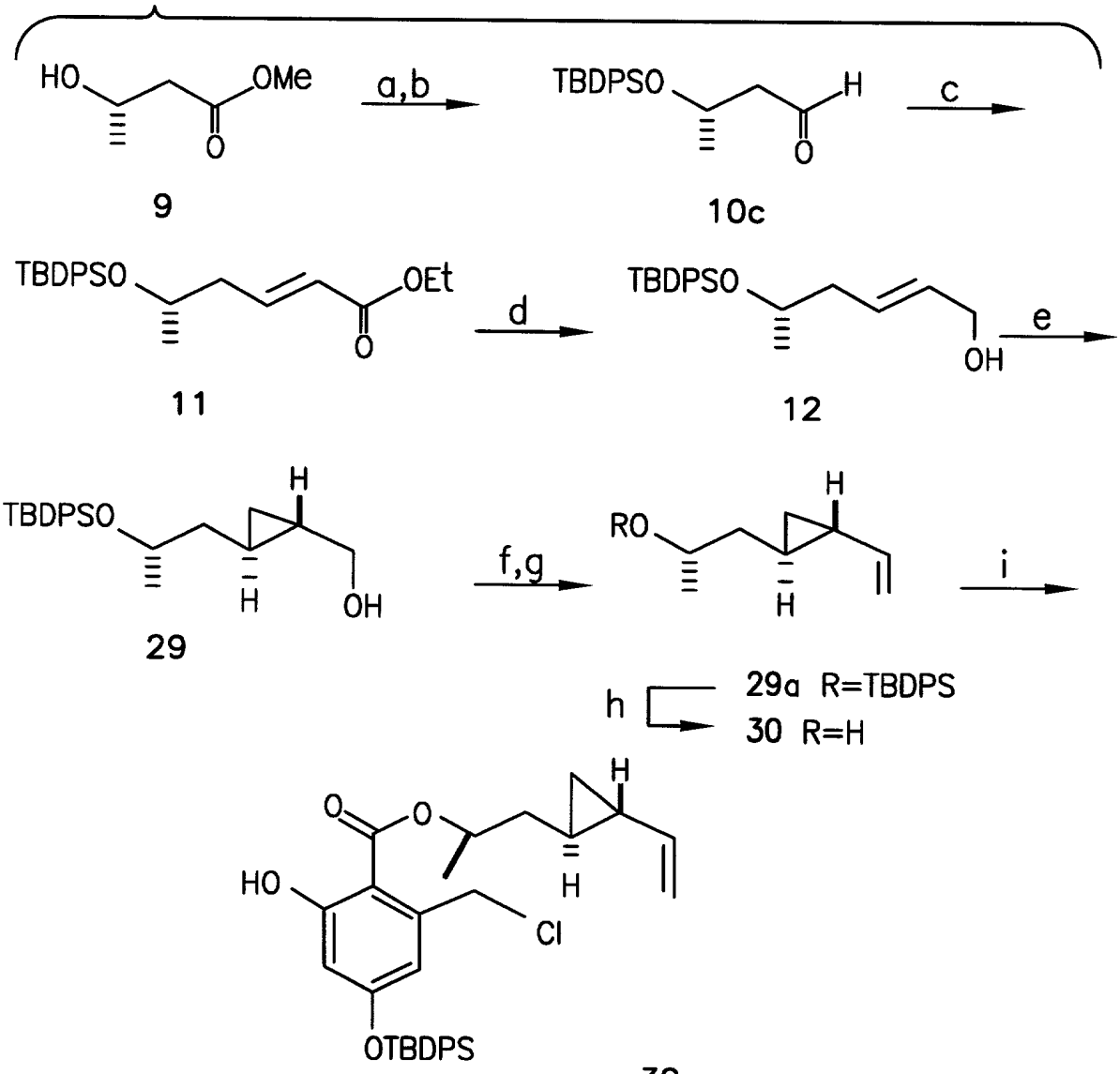


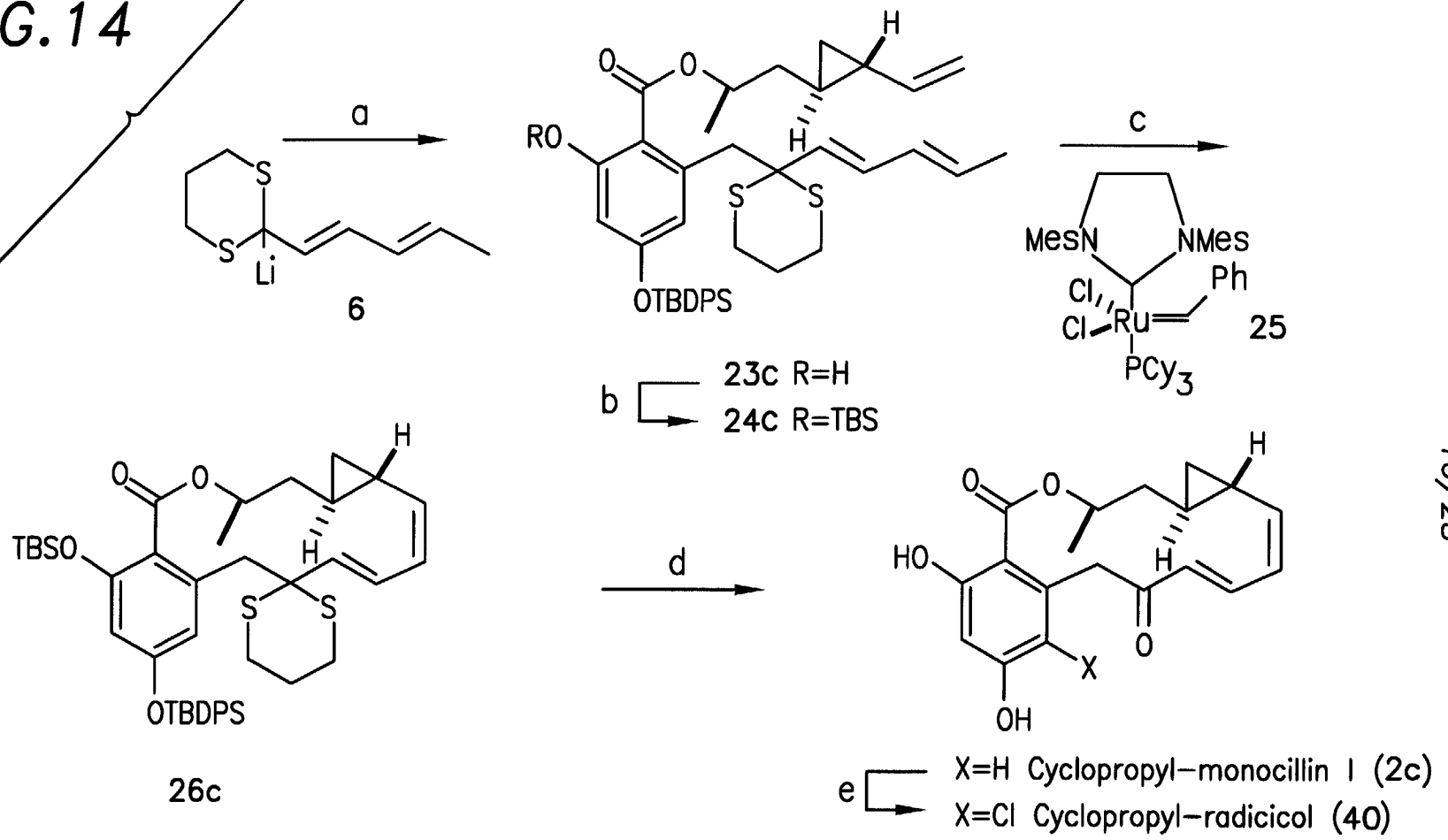
FIG. 13



39

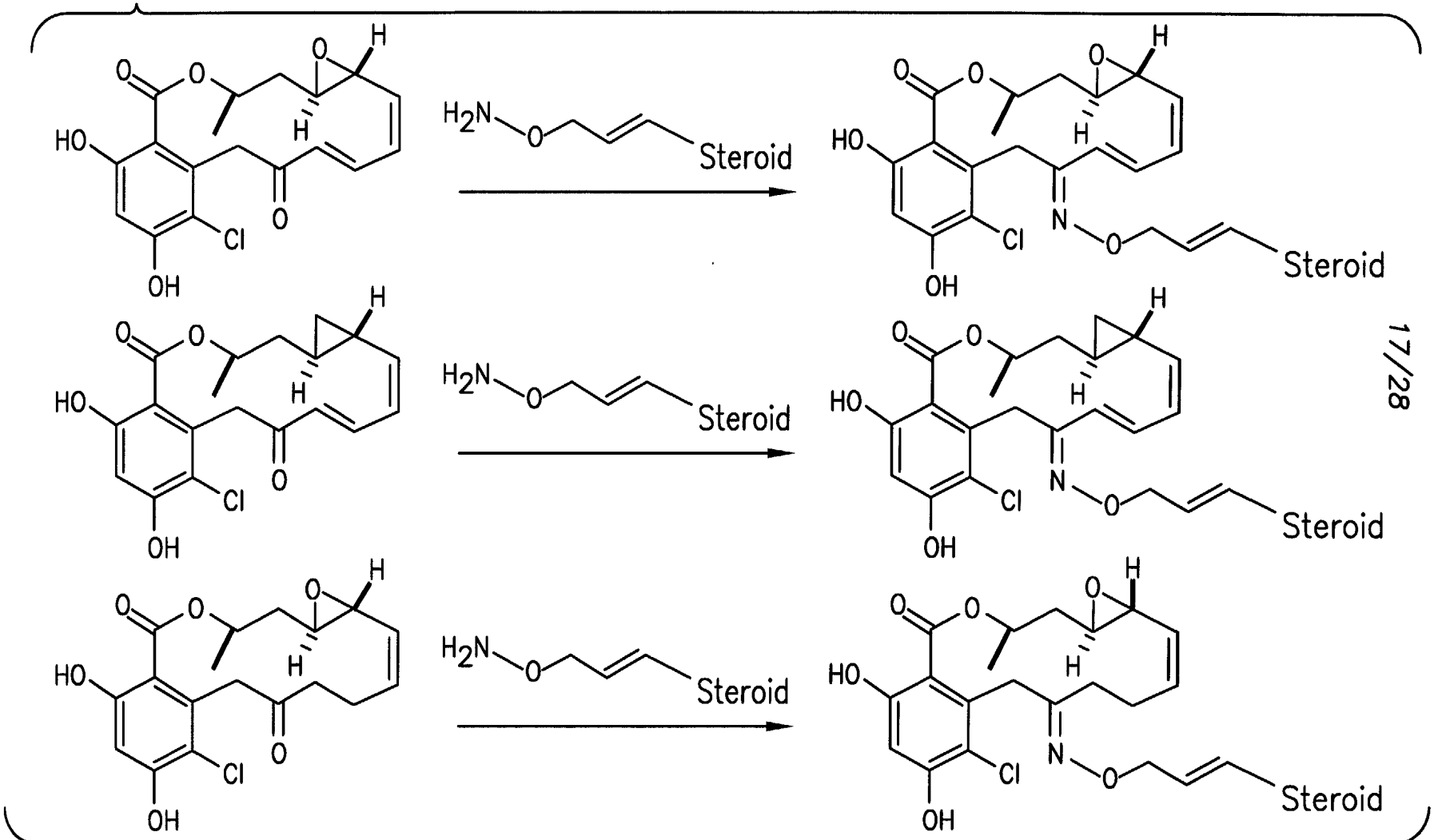
[a] (a) TBDPSCl, imid.,>95%; (b) DIBAL–H,–78 °C, 92%; (c) LiCl, DIPEA $(EtO)_2P(O)CH_2CO_2Et$, 95%; (d) DIBAL–H –20 °C, 96%; (e) (+)–tetramethyltartaricacid diamide–BBu, Et_2Zn, CH_2I_2, 9 >95% ee; (f) SO_3*pyridine, Et_3N, DMSO, 90%; (g) Ph_3 PCH NaHMDS, 0 °C, 82%; (h) TBAF, 89%; (i) 7, P(furyl)$_3$, DIA benzene, 60%

FIG. 14



a. n–BuLi, –78 °C, 75% (3:1); b. TBSCl, 83%; c. 42 °C, 20%; d. (i) mCPBA, (ii) Ac_2O, Et_3N, H_2O, 60 °C, (iii) $NaHCO_3$, MeOH, 60%; e. SO_2Cl_2, 80%

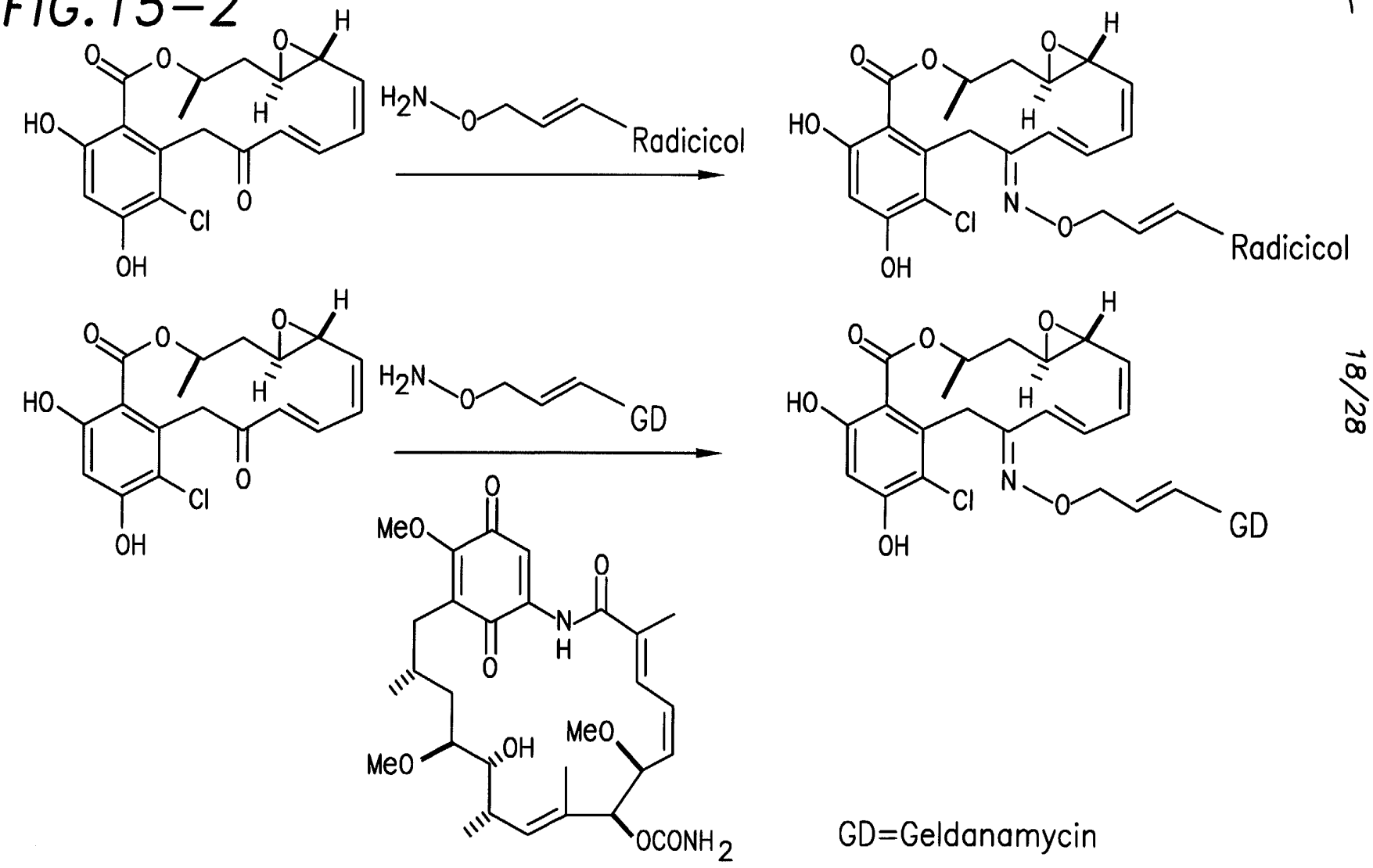
FIG. 15-1



TO FIG. 15-2

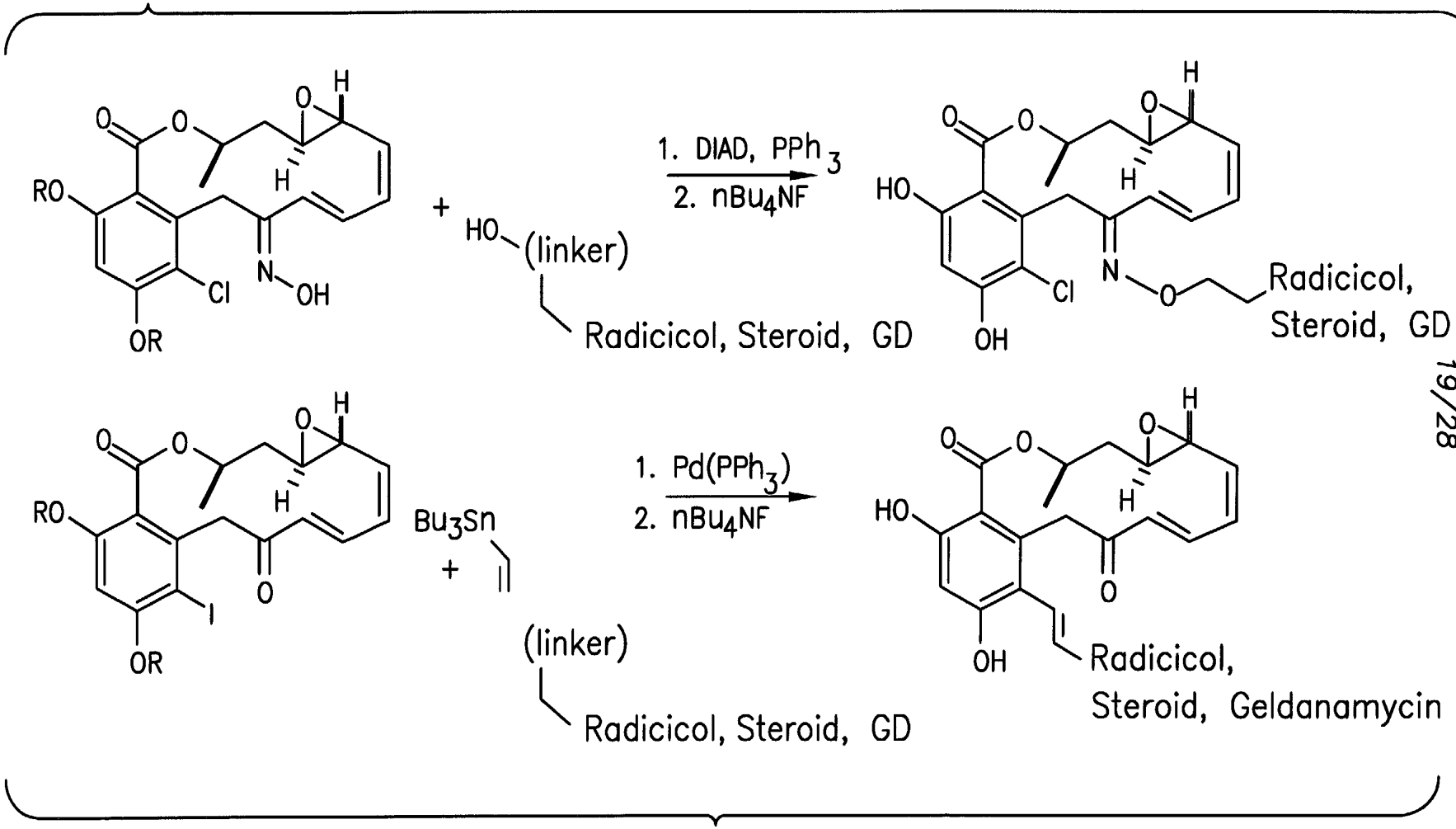
FROM FIG. 15-1

FIG. 15-2



GD=Geldanamycin

FIG. 16-1



TO FIG. 16-2

FROM FIG. 16-1

FIG. 16-2

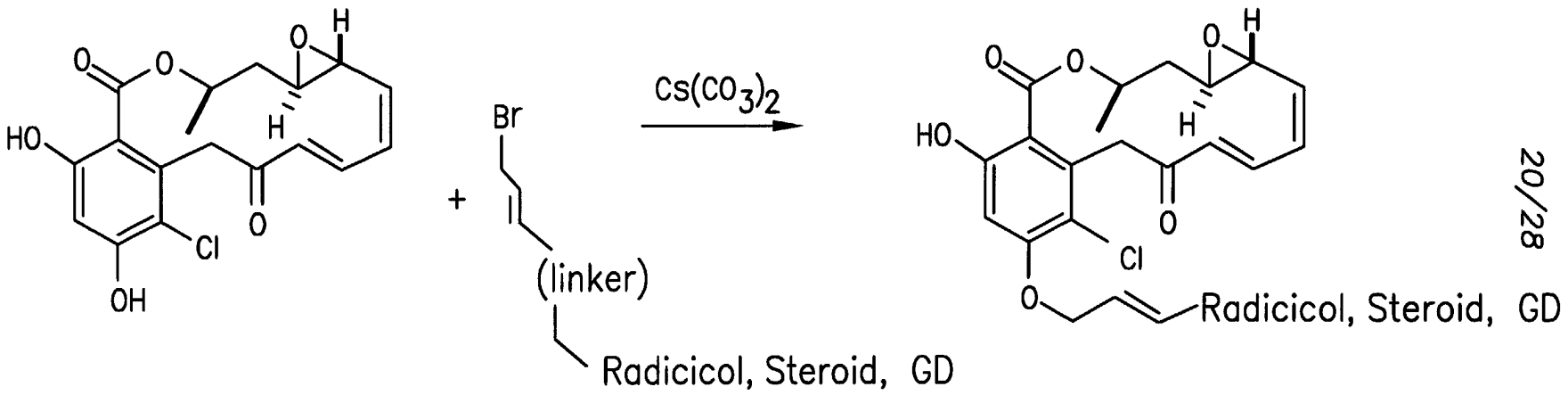
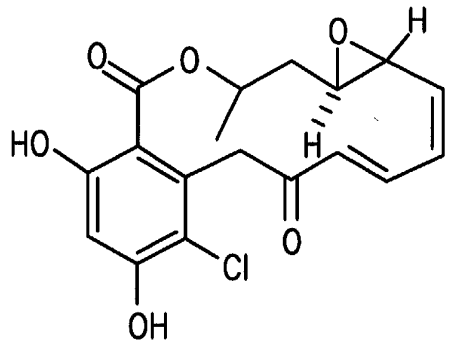
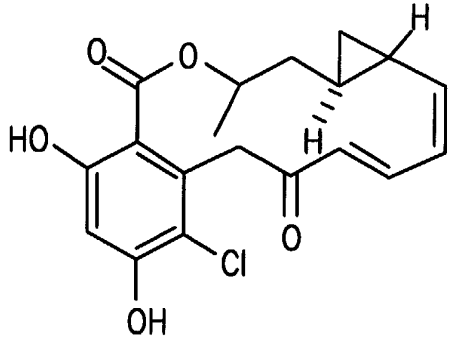


FIG. 17-1

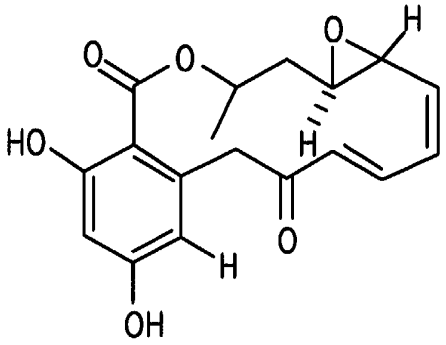
I. Radicicol



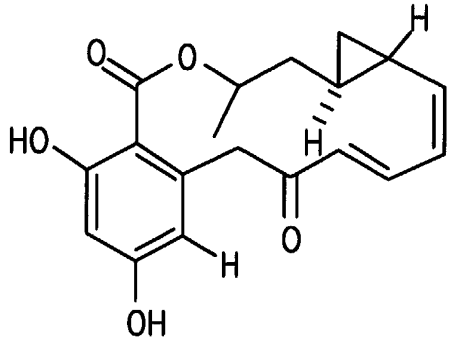
III. Cyclopropyl radicicol



II. Monocillin I



IV. Cyclopropyl monocillin



TO FIG. 17-2

FROM FIG. 17-1

FIG. 17-2

MCF7 Cells Treated with Radicicol and Analogues

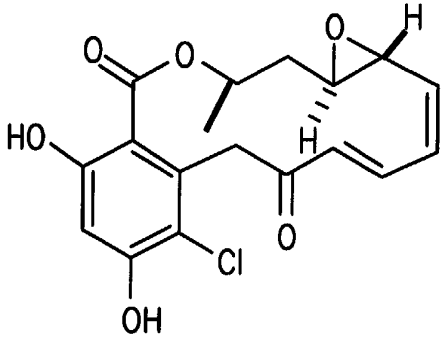
HER2

TO FIG. 17-3

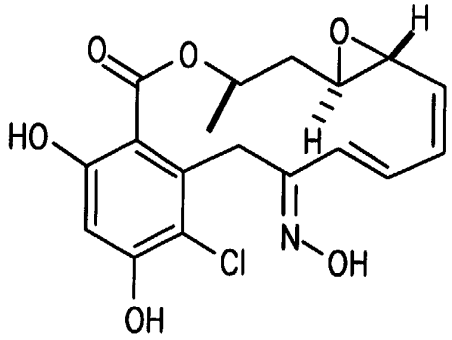
FROM FIG. 17-2

FIG. 17-3

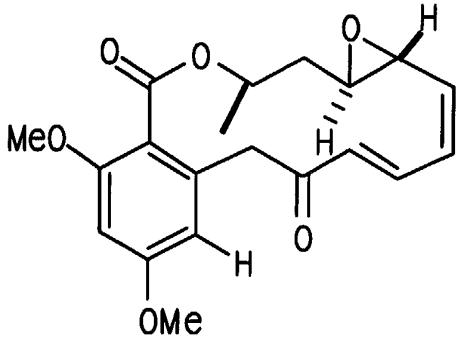
I. Radicicol



VII. Radicicol Oxime



V. Dimethyl Monocillin I



VI. Dimethyl Radicicol

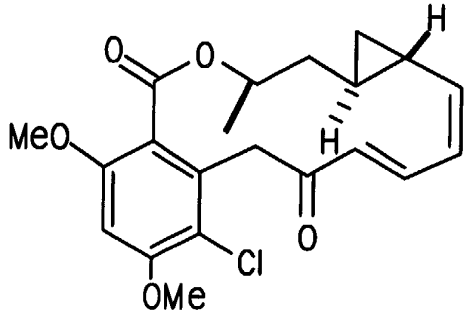
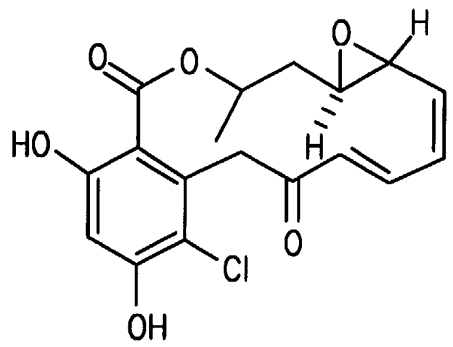
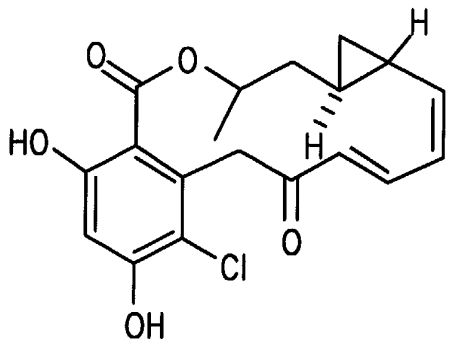


FIG. 18-1

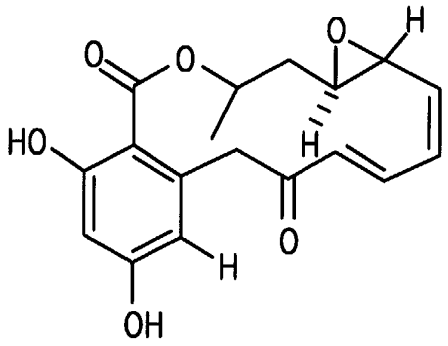
I. Radicicol



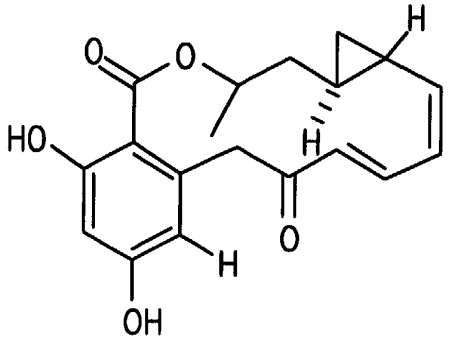
III. Cyclopropyl radicicol



II. Monocillin I



IV. Cyclopropyl monocillin

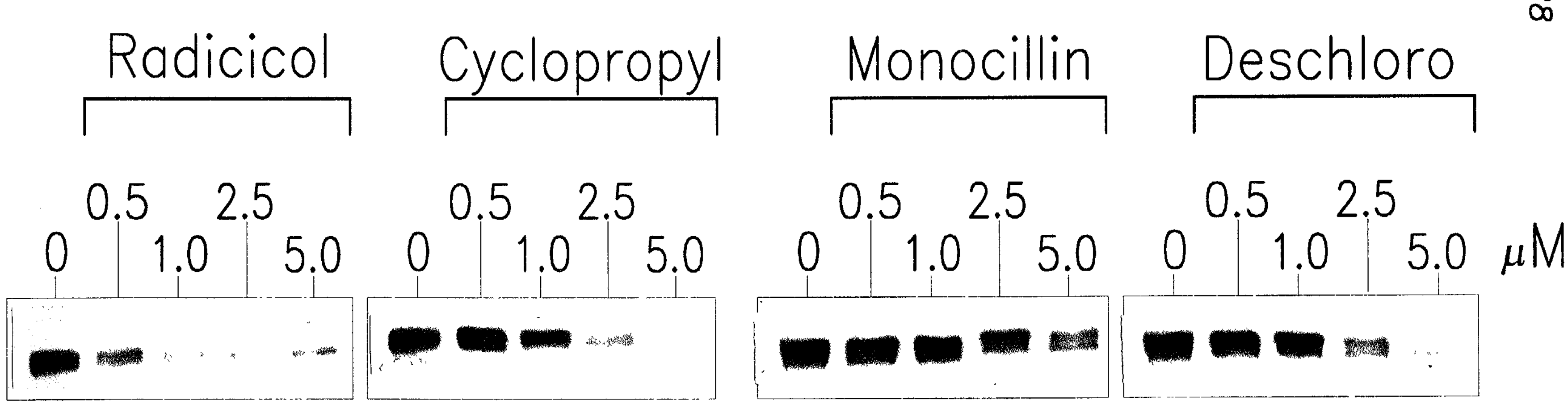


TO FIG. 18-2

FROM FIG. 18-1

FIG.18-2

BT474 Cells Treated with Novel Radicicols (24hrs.)



HER2

FIG. 19

Growth of MCF7 Treated with Radicicol and Derivatives of Radicicol

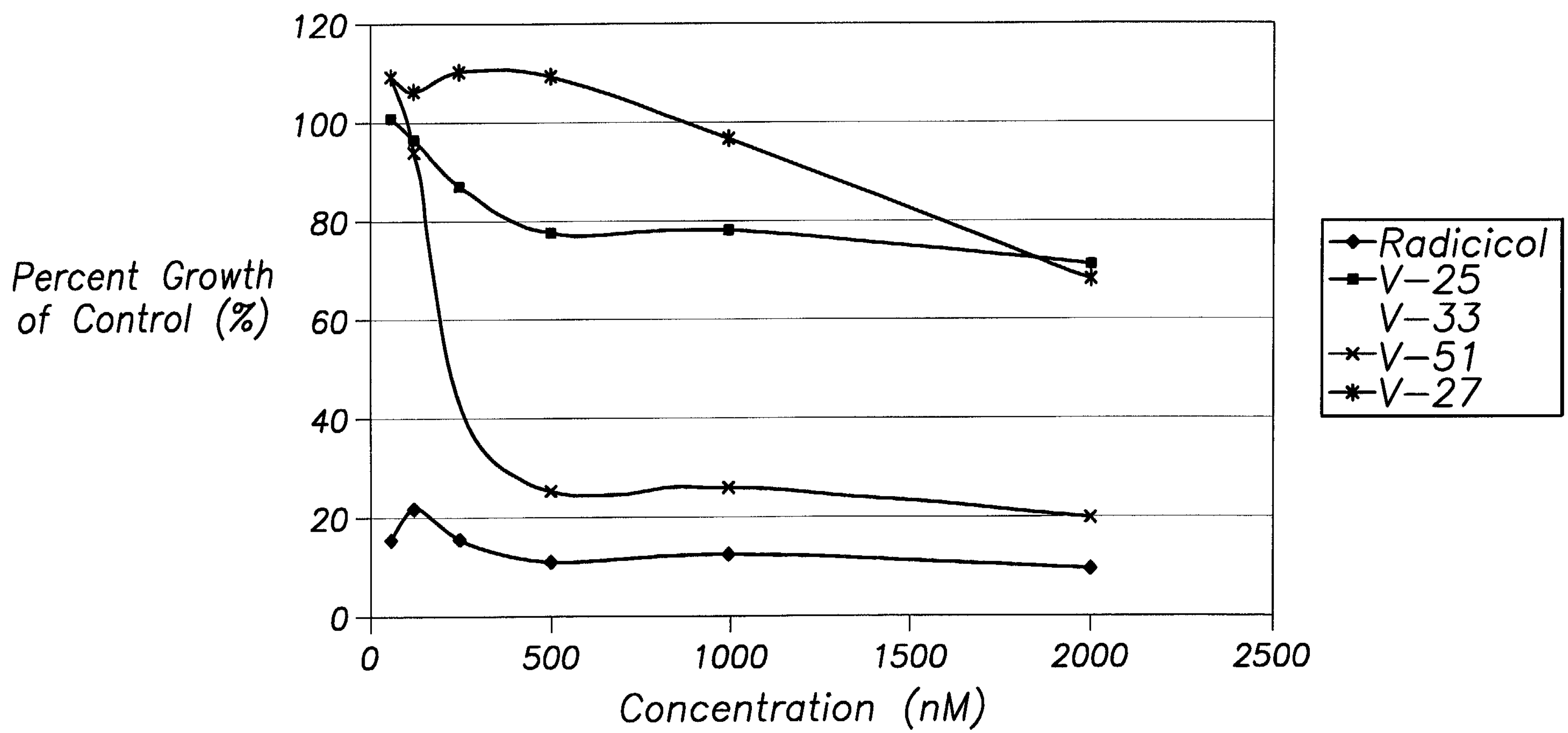


FIG.20

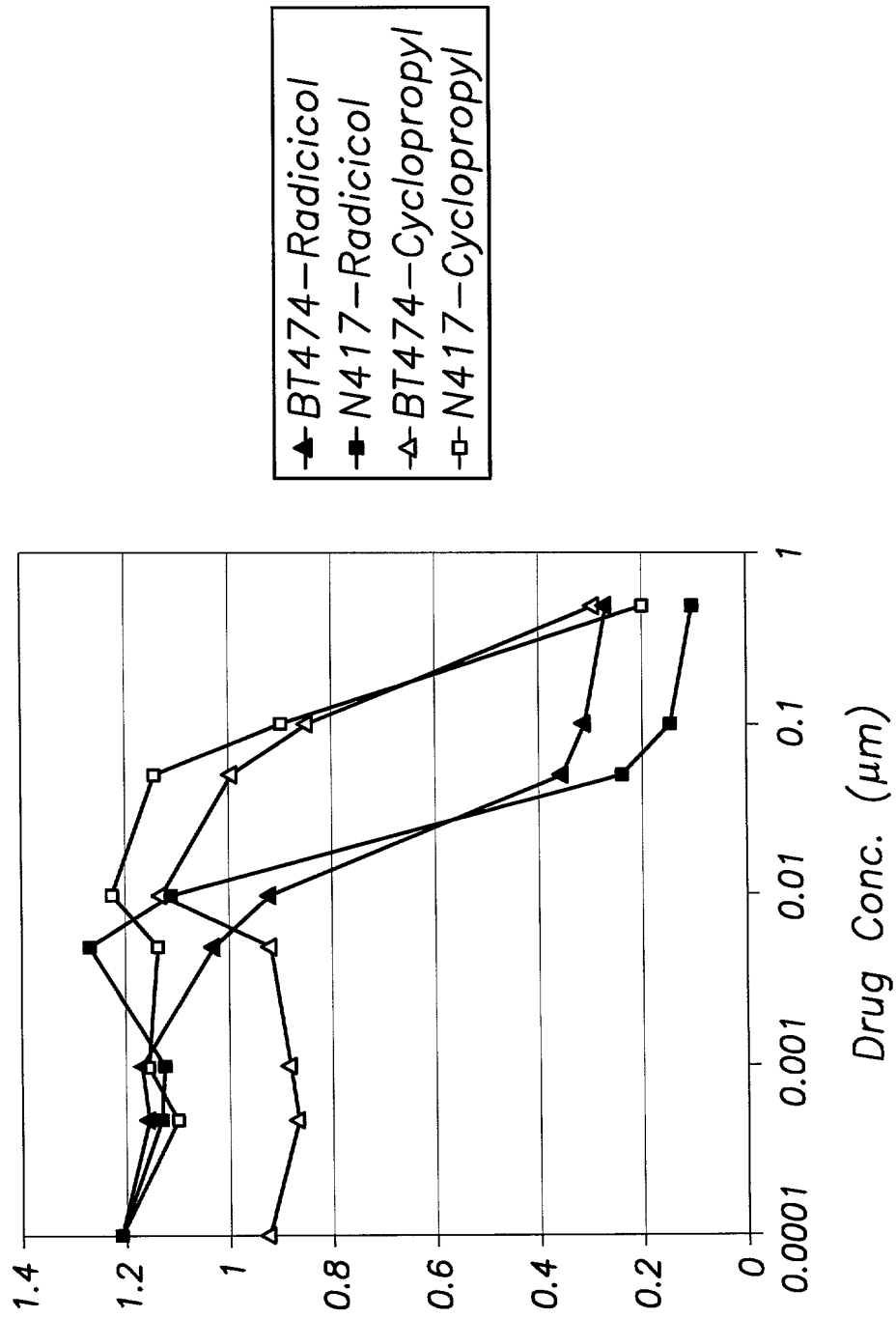
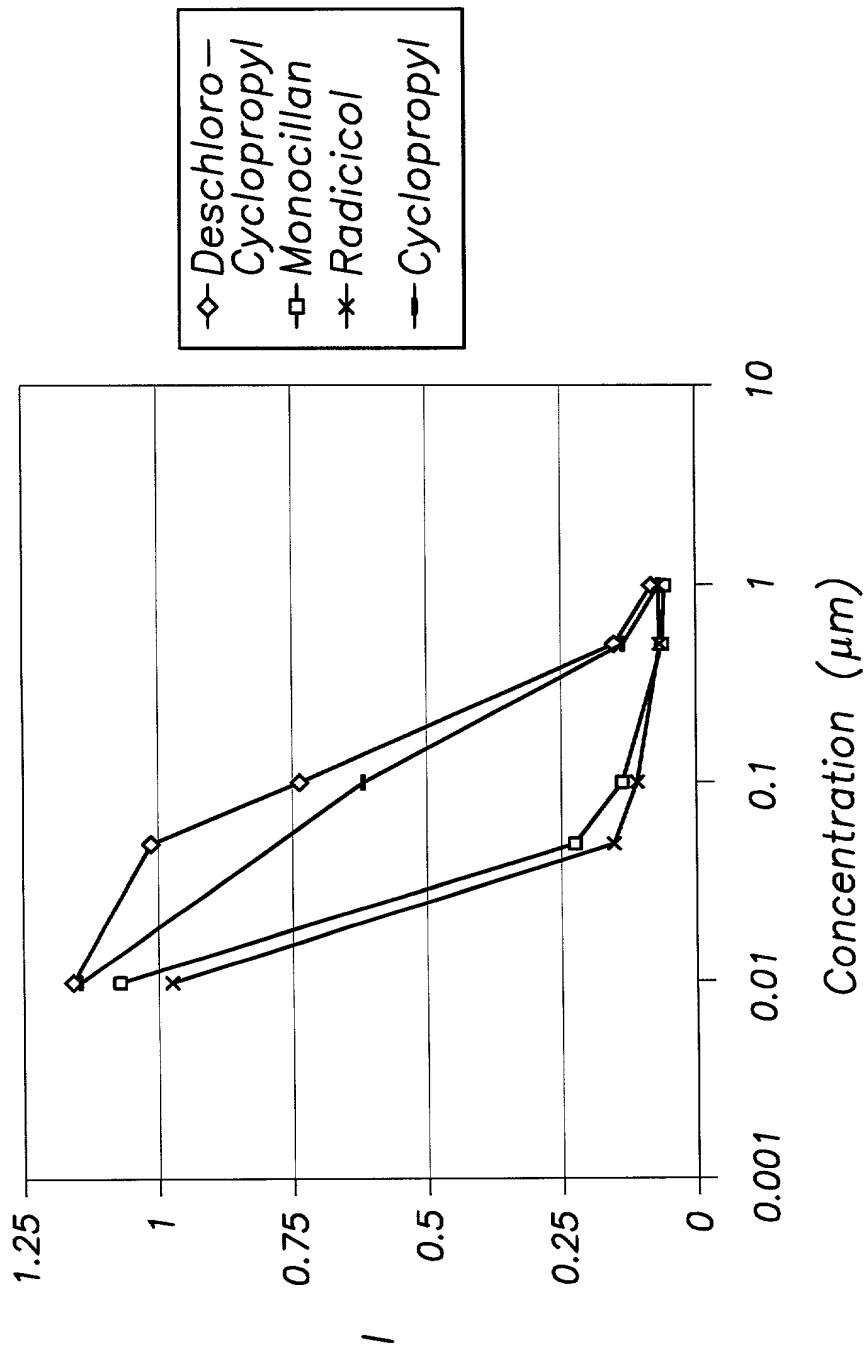

BT474–Radicicol
N417–Radicicol
BT474–Cyclopropyl
N417–Cyclopropyl
% Control
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0.0001
0.001
0.01
0.1
1
Drug Conc. (μm)

FIG.21


N417
Deschloro–Cyclopropyl
Monocillan
Radicicol
Cyclopropyl
% Control
1.25
1
0.75
0.5
0.25
0
0.001
0.01
0.1
1
10
Concentration (μm)